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Certificate

This is to certify that

Dr. Pavan Vijay Raut

Dept. of Chemistry, Smt. Radhabai Sarda Arts, Commerce and Science College, Anjangaon Surji has participated and delivered Invited Talk / Chaired Technical Session / Presented Paper on Topic / Title: 'A Novel Synthesis of 2-[2-(2, 6- SUBSTITUTEDDITHIOCARBAMIDO-ANILINO) PHENYL] Acetic Acid ' in the

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A NOVE SYNTHESIS OF 2-[2-(2,6-SUBSTITUTEDDITHIOCARBAMIDO - ANILINO)PHENYL] ACETIC ACID

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Abstract

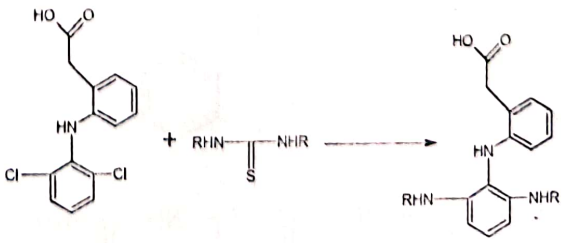
Thicarbamido, Thioamido and Triazino group containing heterocycles and heteroacycles created their own identity and importance in pharmaceutical, medicinal, agricultural and drug sciences. Thiocarbamido heteroacyclic compounds showed noticeable and remarkable applications in industrial, pharmaceutical, medicinal and drug chemistry. Hence taking all these facts into consideration it was thought interesting to investigate the interactions of 2-[2-(2,6-dichloroanilino) phenyl] acetic acid with substitutedthiocarbamide (2a-e) in isopropanol medium to isolate 2-[2-(2,6-substituteddithiocarbamidoanilino) phenyl] acetic acid. The synthesised compound were characterised on the basis of conventional and elemental analysis, chemical characteristics and through IR and NMR spectral studies.

INTRODUCTION

The literature survey of 2-[2-(2,6-dichlorooanilino)phenyl]acetic acid compound is generally use as anti-fertility and anti-tumor agent having minimum side effect. The literature survey of thiocarbamide also shows that the thiocarbamido nucleus containing drug have their own importance in pharmaceutical chemistry because thus drug show anti-inflammatory, Analgesic, anti-emetic and Anti-rhematic properties. The clinical pharmacology, pharmacokinetics, contraindication, NMS, adverse, reaction, drug interaction, uses of diclofenac was studied in sufficient details. 2-[2-(2,6-dichloroanilino)phenyl]acetic acid is known as diclofenac [1-11]. It is use as the anti-inflammatory drug and thiocarbamide nucleus contain various medicinal and pharmaceutical applications[12].

As wider program of this laboratory in the synthesis of nitrogen and sulphur containing heterocycles and their cyclisation into 5,6, and 7 membered heterocyclic and to investigate their medicinal, pharmaceutical parameters, it was thought interesting to carry out the interactions of 2-[2-(2,6-dichloroanilino)phenyl]acetic acid with substituted thiocarbamide (2a-e) in isopropanol medium to isolate a new series of heterocyclic drugs having aniline and thiocarbamide nucleus in the same drug. This drug may enhance the potency of drug and may also introduce new type of drug activity. In this drug this type of reaction are heither to unknown .This synthetic approach will become a milestone and open a new path in pharmaceutical, biochemical, medicinal and drug chemistry.

Taking all this thinking into consideration the interactions of 2-[2-(2,6-dichloroanilino)phenyl]acetic acid with substituted thiocarbamide (2a-e) in isopropanol medium[13-15]. **(Scheme-I)**



Scheme-1

RESULT AND DISCUSSION

Synthesis of 2-[2-(2,6-dithiocarbamidoanilino)phenyl]acetic acid (3a)

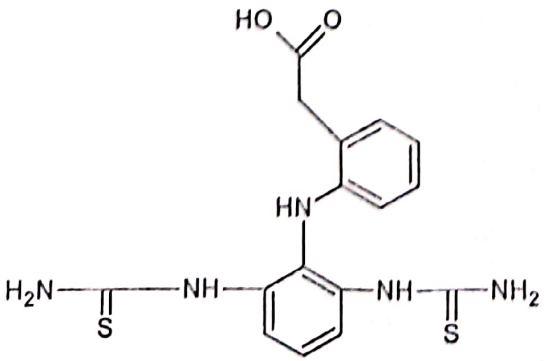
A mixture 2-[2-(2,6-dichloroanilino)phenyl]acetic acid, thiocarbamide and isopropanol (40ml) was refluxed on boiling water bath for 4 hrs. During boiling suspended 2-[2-(2,6-dichloroanilino)phenyl]acetic acid went into the solution and the new product was found to be gradually separated out which on basification with dilute ammonium hydroxide afforded crystals. It was filtered in hot condition and crystallized with aqueous ethanol to obtain **(3a)**, yield 87.8% and melting point 169°C.

The compound is white and crystalline in nature and having melting point 169°C. It contains nitrogen and sulphur. It did not give test for chlorine it means that chlorine is removed during refluxed. Desulphurised with alkaline plumbite solution. Form picrate having melting point 147°C.

IR Spectra[13-15]:-The IR spectra was carried out in KBr pellets and reproduced on IR plate number HS-1. The important absorption in cm^{-1} are N-H Stretching 3394.22, C-H Stretching 2914.43, C-N Stretching 1130.29, -C=O Stretching 1627.92 and -C=S Stretching 669.30 and OH Stretching .

PMR Spectra[13-15]:-The spectrum was carried out in $CDCl_3$. This spectrum distinctly displayed the signals due to Ar-H protons at δ 6.2659-7.5352 ppm, $-NH_2$ protons at δ 4.1034-4.1460, -NH at δ 3.3573-3.7924 ppm, $-CH_2$ at δ 1.1691-1.4097 ppm and –OH at δ 0.8384-0.8657 ppm.

From the above properties and the spectral analysis the compound (3a) was assigned the structure as 2-[2-(2,6-dithiocarbamidoanilino) phenyl]acetic acid.



Similarly methyl, ethyl, allyl and phenylthiourea (2b-e) were interacted with 2-[2-(2,6-dichloroanilino)phenyl]acetic acid in isopropanol medium respectively by the above mentioned method in Experiment No. 2.

EXPERIMENTAL

The melting point of all the synthesized compounds was recorded using hot paraffin bath. IR spectra were recorded on Shemadzu spectrometer in the range 4000-400 cm^{-1} in KBr pellet's. PMR spectra were recorded Bruker AC -500F spectrometer with TMS as internal standard using $CDCl_3$ and DMSO as solvent. The purity of compounds was checked on Silica-gel-g plates by TLC within the layer thickness of 0.3 mm. All used were of AR Grade.

EXPERIMENT-2

Synthesis of 2-[2-(2,6-dimethylthiocarbamidoanilino)phenyl]acetic acid (3b)

A mixture 2-[2-(2,6-dichloroanilino)phenyl]acetic acid, methylthiocarbamide and isopropanol (40ml) was refluxed on boiling water bath for 4 hrs. During boiling suspended 2-[2-(2,6-dichloroanilino)phenyl]acetic acid went into the solution and the new product was found to be gradually separated out which on basification with dilute ammonium hydroxide afforded crystals. It was filtered in hot condition and crystallized with aqueous ethanol to obtain **(3b)**, yield 85.00 % and melting point 161°C.

EXPERIMENT-3

Synthesis of 2-[2-(2,6-diethylthiocarbamidoanilino)phenyl]acetic acid (3c)

A mixture 2-[2-(2,6-dichloroanilino)phenyl]acetic acid, ethylthiocarbamide and isopropanol (40ml) was refluxed on boiling water bath for 4 hrs. During boiling suspended 2-[2-(2,6-dichloroanilino)phenyl]acetic acid went into the solution and the new product was found to be gradually separated out which on basification with dilute ammonium hydroxide afforded crystals. It was filtered in hot condition and crystallized with aqueous ethanol to obtain **(3c)**, yield 87.00 % and melting point 165°C.

EXPERIMENT-4

Synthesis of 2-[2-(2,6-diallylthiocarbamidoanilino)phenyl]acetic acid (3d)

A mixture 2-[2-(2,6-dichloroanilino)phenyl]acetic acid, allylthiocarbamide and isopropanol (40ml) was refluxed on boiling water bath for 4 hrs. During boiling suspended 2-[2-(2,6-dichloroanilino)phenyl]acetic acid went into the solution and the new product was found to be gradually separated out which on basification with dilute ammonium hydroxide afforded crystals. It was filtered in hot condition and crystallized with aqueous ethanol to obtain **(3d),** yield 79.00 % and melting point 173^{0}C.

EXPERIMENT-5

Synthesis of 2-[2-(2,6-diphenylthiocarbamidoanilino)phenyl]acetic acid (3e)

A mixture 2-[2-(2,6-dichloroanilino)phenyl]acetic acid, phenylthiocarbamide and isopropanol (40ml) was refluxed on boiling water bath for 4 hrs. During boiling suspended 2-[2-(2,6-dichloroanilino)phenyl]acetic acid went into the solution and the new product was found to be gradually separated out which on basification with dilute ammonium hydroxide afforded crystals. It was filtered in hot condition and crystallized with aqueous ethanol to obtain **(3e),** yield 87.00 % and melting point 185^{0}C.

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